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Biomimetic Total Synthesis of (±)-Doitunggarcinone A and (+)-Garcibracteatone

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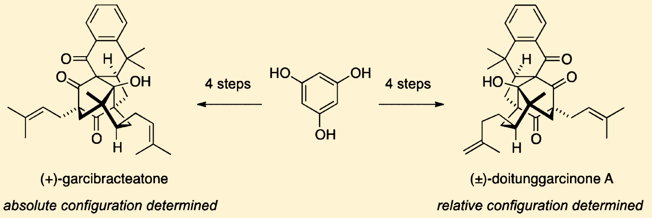
Supporting Information

ABSTRACT: A full account of our oxidative radical cyclization approach to the synthesis of garcibracteatone and doitunggarcinone A is presented. This includes the first enantioselective synthesis of garcibracteatone, which allowed the absolute configuration of the natural compound to be determined. The first synthesis of doitunggarcinone A is also described, which confirms our reassignment of the relative configuration of this molecule. Novel syntheses of monoterpene fragments used to construct the target molecules are also reported.



INTRODUCTION

Polycyclic polyprenylated acylphloroglucinols (PPAPs) are a large and structurally diverse family of plant-derived natural products. The chemistry and biology of these compounds has been summarized in several recent reviews,[1] and there are many successful total syntheses of PPAP natural products.[2] Most PPAPs contain a bicyclo[3.3.1]nonane ring system, which is proposed to be biosynthesized via electrophilic cyclizations of monocyclic polyprenylated acylphloroglucinols.[3] However, we believe that many of the more complex PPAP natural compounds, such as garcibracteatone (**1**),[4] nemorosonol (**3**),[5] doitunggarcinone A (**2**), doitunggarcinone B (**4**),[6] ialibinone A (**5**), ialibinone B (**6**),[7] and peroxysampsone A (**7**)[8] are formed in nature via oxidative radical cyclizations (Figure 1). Porco has previously shown that oxidative radical cyclizations can be used to build up complex unnatural PPAP structures,[9] and we have previously used an oxidative radical cyclization approach in the synthesis of (±)-ialibinones A (**5**) and B (**6**).[10] Herein, we give a full account of our biomimetic syntheses of (+)-garcibracteatone (**1**)[11] and (±)-doitunggarcinone A (**2**).

Garcibracteatone and nemorosonol were co-isolated from *Garcinia bracteata*, while doitunggarcinones A and B were co-isolated from *Garcinia propinqua*, thus suggesting a close biogenetic relationship within these pairs of natural products. Our proposed biosynthesis of garcibracteatone, nemorosonol, and doitunggarcinones A and B is outlined in Scheme 1. The starting point for the radical cyclization pathways are the dearomatized compounds **8** and **9**, which could be formed by multiple prenylations of acylphloroglucinol derivatives. Compound **8** is a possible diastereomer of weddellianone A,[12] a known acylphloroglucinol natural product isolated from *Clusia weddelliana*, but whose relative and absolute configurations have not been fully established. Single electron oxidation of compound **8** or **9** would give rise to a stabilized α-diketo radical, which could undergo successive 7-*endo-trig* and 5-*exo-trig* cyclizations followed by hydrogen atom abstraction to give nemorosonol (**3**) or doitunggarcinone B (**4**). Alternatively, a second 5-*exo-trig* cyclization followed by an aromatic radical substitution reaction would give rise to garcibracteatone (**1**) or doitunggarcinone A (**2**). Although this biosynthetic pathway constitutes a highly complex sequence of reactions, we reasoned that the compact nature of the radical intermediates

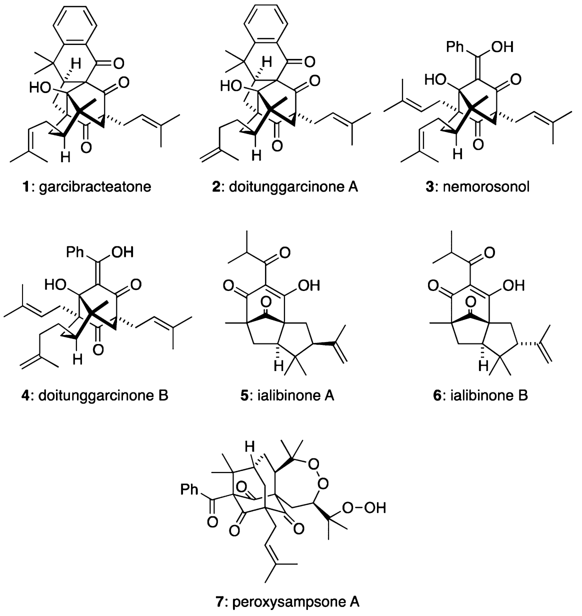


Figure 1. PPAP natural products possibly biosynthesized by radical cyclizations.

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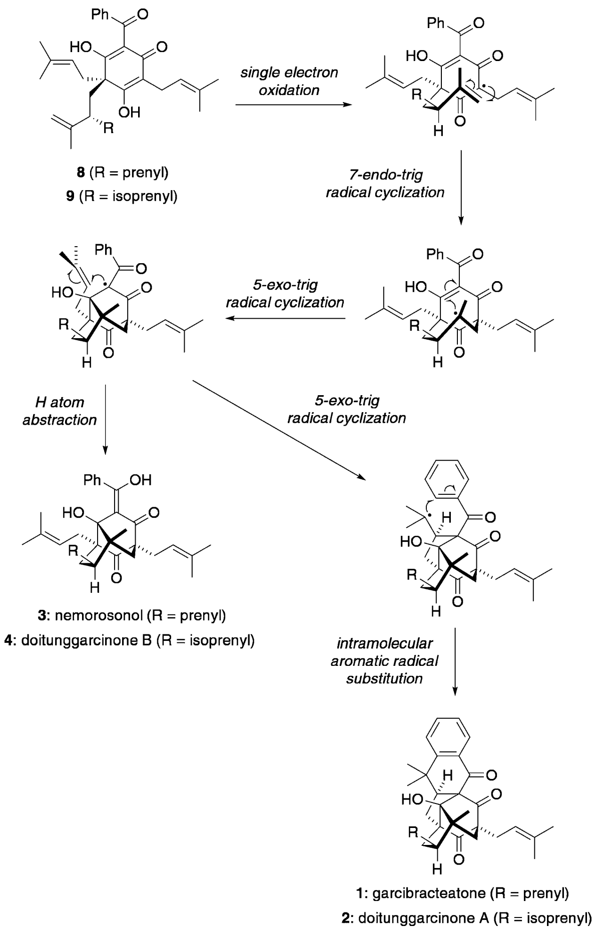
Scheme 1. Proposed Biosynthesis of Garcibracteatone, Nemorosonol, and Doitunggarcinones A and B

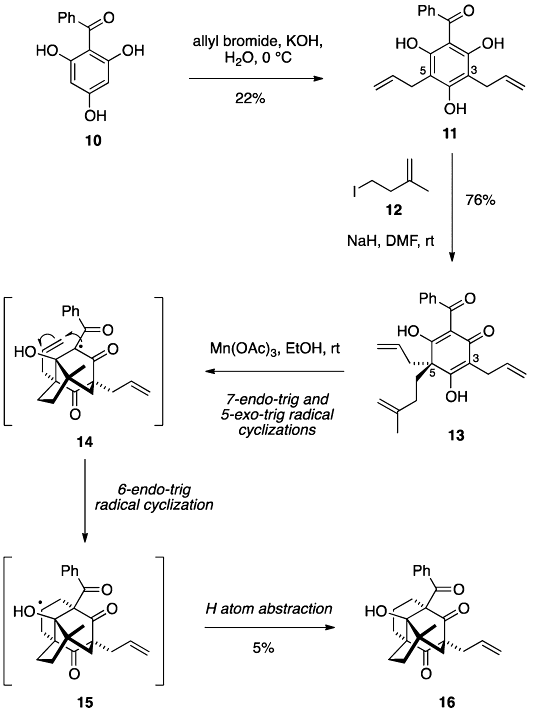


might render the cyclizations predisposed to occur under nonenzymatic conditions in a biomimetic synthesis.

■ RESULTS AND DISCUSSION

We initially investigated the feasibility of a radical cyclization approach to PPAP synthesis through some model studies using the dearomatized phloroglucinol **13** as a simplified analogue of **8** or **9** (Scheme 2). The use of a 2-methyl-1-butene substituent at C-5 instead of the natural lavandulyl side chain simplified the system considerably, and the presence of allyl groups at C-3 and C-5 instead of prenyl groups would be expected to reduce the possibility of competing 5-*exo-trig* cyclizations (as observed in our biomimetic synthesis of ialibinones A and B). Thus, 2,4,6-trihydroxybenzophenone (**10**)[13] was allylated at C-3 and C-5 using allyl bromide in aqueous KOH to give **11** in 22% yield. Dearomatization of **11** with NaH and 4-iodo-2-methyl-1-butene (**12**)[14] in DMF gave **13** in good yield. Oxidation of **13** using $Mn(OAc)_3$[15] in EtOH then gave **16** as the only isolable product, in low yield of 5%. Presumably **16** was formed via oxidative 7-*endo-trig* and 5-*exo-trig* cyclizations common to the proposed biosynthesis outlined in Scheme 1 to form the α-diketo radical **14**. However, this radical apparently underwent an unexpected final 6-*endo-trig* cyclization onto the C-5 allyl group to give the secondary radical **15**, followed by a terminating hydrogen atom abstraction step to give **16**. We had hoped that the α-diketo radical intermediate **14** might undergo hydrogen atom abstraction itself, thereby forming the polycyclic ring system common to nemorosonol (**3**) and doitunggarcinone B (**4**).

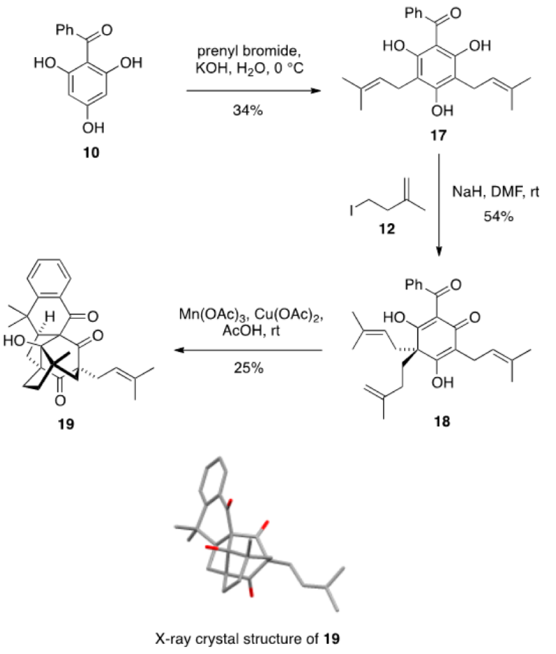
Scheme 2. Model Oxidative Cyclization Studies



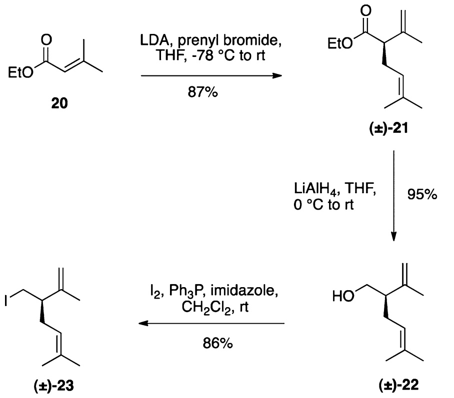
Although the oxidative radical cyclization of **13** did not proceed as planned, we were encouraged that the initial 7-*endo-trig* and 5-*exo-trig* cyclizations had apparently worked to some degree. We reasoned that replacement of the allyl groups of **13** with prenyl groups might encourage a diketo radical such as **14** to undergo a second 5-*exo-trig* cyclization, rather than a 6-*endo-trig* cyclization. A terminating intramolecular aromatic radical substitution reaction might then form the polycylic framework of garcibracteatone (**1**) and doitunggarcinone A (**2**). Thus, 2,4,6-trihydroxybenzophenone (**10**) was reacted with prenyl bromide in aqueous KOH to give **17** in 34% yield (Scheme 3).[16] Dearomatization of **17** with NaH and 4-iodo-2-methyl-1-butene (**12**) in DMF then gave **18** in 54% yield. Treatment of **18** with $Mn(OAc)_3$ and $Cu(OAc)_2$ in AcOH gave **19** in 25% yield via a radical cyclization cascade that formed the complete garcibracteatone/doitunggarcinone A framework in one step, presumably via the mechanism outlined in Scheme 1. The low yield of 25% is compensated by the formation of four carbon–carbon bonds and five stereocenters in the reaction, with complete control of relative stereochemistry. The structure of **19** was elucidated by NMR studies, with the ^1H and ^{13}C NMR spectra showing close similarity to those of natural garcibracteatone (**1**) and doitunggarcinone A (**2**). The structure of **19** was later confirmed by X-ray crystallographic studies.[17] No products containing the nemorosonol/doitunggarcinone B ring system were observed during either of these model studies. Screening of a variety of alternative one-electron oxidants, such as $PhI(OAc)_2$, $PhI(OTf)_2$, and CAN, failed to generate any detectable quantities of **19**.

In order to apply the radical cyclization cascade to a full total synthesis of (±)-garcibracteatone ((±)-**1**), we now needed to alkylate **17** with (±)-lavandulyl iodide ((±)-**23**), which could be obtained by iodination of (±)-lavandulol ((±)-**22**, Scheme 4). Although (±)-lavandulol is commercially available, we had

Scheme 3. Model Oxidative Cyclization Studies



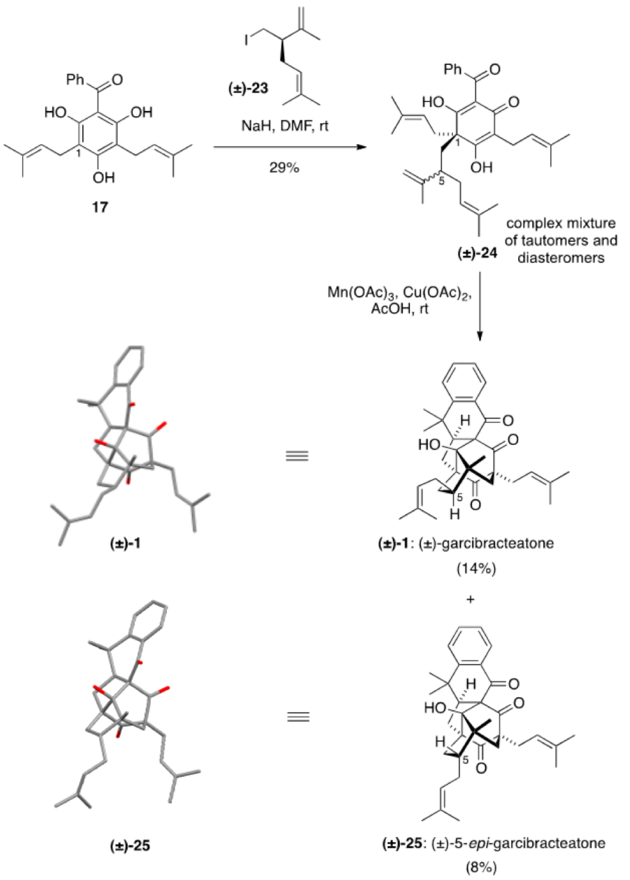
Scheme 4. Synthesis of (±)-Lavandulyl Iodide



difficulty obtaining it cheaply, and we therefore developed an efficient and economical synthesis from ethyl 3,3-dimethylacrylate (**20**). Deprotonation of **20** with LDA in THF followed by α-alkylation with prenyl bromide gave (±)-**21** in high yield, with concomitant shift of the alkene from the α,β to the β,γ position. The ethyl ester of (±)-**21** was then reduced using $LiAlH_4$ to give (±)-lavandulol ((±)-**22**) in excellent yield.[18] Iodination of (±)-**22** under standard conditions then gave (±)-**23** in 86% yield.

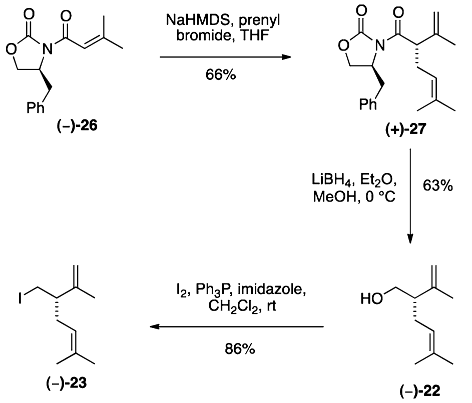
Alkylation of **17** with (±)-**23** in DMF with NaH as the base gave (±)-**24** in 29% yield as a complex mixture of enol tautomers and diastereomers, as the relative C-1/C-5 stereochemistry (using garcibracteatone numbering) was not controlled during the reaction (Scheme 5). The yield for the alkylative dearomatization was low due to the sterically hindered nature of the alkyl iodide and competing E2 elimination. However, oxidative cyclization of (±)-**24** using $Mn(OAc)_3$ and $Cu(OAc)_2$ in AcOH gave (±)-garcibracteatone ((±)-**1**) in 14% yield and (±)-5-*epi*-garcibracteatone ((±)-**25**) in 8% yield, which were separable by flash chromatography on silica gel. The mechanism of the oxidative cyclization of (±)-**24** presumably follows the radical cascade outlined in Scheme 1. X-ray crystallographic studies of (±)-**1** and (±)-**25** confirmed their structures, and comparison with the NMR data for the natural material allowed us to confirm the previously undefined C-5 relative configuration of (±)-garcibracteatone to be as shown in Scheme 5.

Scheme 5. Synthesis of (±)-Garcibracteatone



Our next target was an enantioselective synthesis of garcibracteatone, which would require access to enantiopure lavandulyl iodide. We therefore synthesized (−)-**23** according to Scheme 6 using a chiral auxiliary approach.[19] Alkylation of (−)-**26**[20] with prenyl bromide and NaHMDS as the base gave (+)-**27** in 66% yield and 15:1 dr. Reduction of (+)-**27** with $LiBH_4$ gave (−)-**22**, which was iodinated to give (−)-**23** under

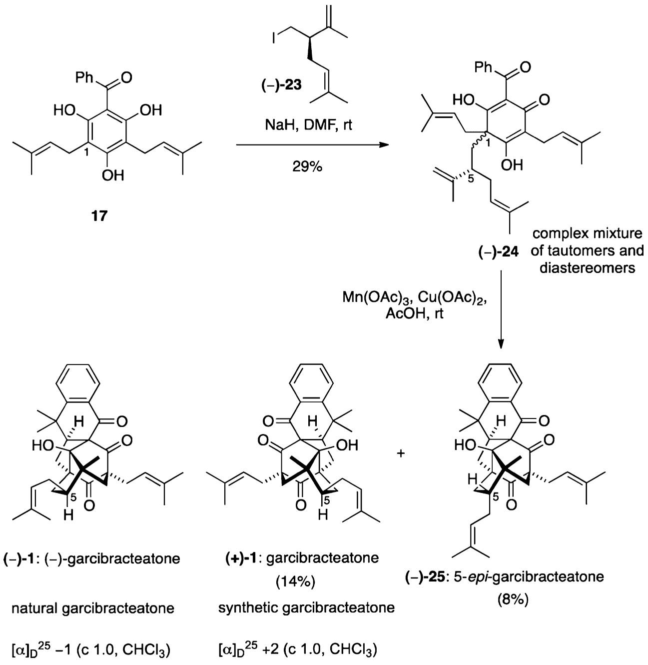
Scheme 6. Enantioselective Synthesis of (−)-Lavandulyl Iodide



standard conditions. This represents a practical synthesis of enantiopure lavandulol and lavandulyl iodide that is significantly shorter than existing methods.[21]

With (−)-lavandulyl iodide in hand, we were able to synthesize the dearomatized phloroglucinol (−)-**24** in enantio-enriched form and then (+)-garcibracteatone ((+)-**1**) and (−)-5-*epi*-garcibracteatone ((−)-**25**) via oxidative radical cyclization (Scheme 7). Naturally occurring (−)-garcibracteatone has a very low specific rotation ($[\alpha]^{25}_{D}$ −1 (*c* 1.0, $CHCl_3$)), and our synthetic (+)-garcibracteatone had a similarly low value ($[\alpha]^{25}_{D}$ +2 (*c* 1.0, $CHCl_3$)). Given these low magnitudes, the signs of the specific rotations of natural and synthetic garcibracteatone are probably within the bounds of experimental error and do not, by themselves, allow the determination of the absolute configuration of natural garcibracteatone. However, we were fortunate to have access to a sample of natural garcibracteatone, and comparison of chiral HPLC traces between this and our synthetic material conclusively showed that we had made the enantiomer of the natural product. We can therefore assign the absolute stereochemistry of natural (−)-garcibracteatone to be as shown in Scheme 7.

Scheme 7. Enantioselective Synthesis of (+)-Garcibracteatone



Shortly after our synthesis of garcibracteatone (**1**) had been completed, the isolation of doitunggarcinone A (**2**) and doitunggarcinone B (**4**) from *Garcinia propinqua* was reported. These natural products have very similar structures to garcibracteatone (**1**) and nemorosonol (**3**), differing only in the position of the carbon−carbon double bond in the C-5 alkyl chain. In addition, they were originally assigned as having the opposite relative configuration at C-5 compared to garcibracteatone (**1**) and nemorosonol (**3**). However, close inspection of the ^1H and ^{13}C NMR data for doitunggarcinone A (**2**) showed very good correlation with the NMR spectra of our synthetic garcibracteatone (**1**), whereas comparison with the NMR spectra of synthetic 5-*epi*-garcibracteatone (**25**) showed significant differences. Similarly, the NMR data for doitunggarcinone B (**4**) are almost identical to those of nemorosonol (**3**). We therefore suggest that structures **2** and **4** represent the correct stereochemical assignment for doitunggarcinones A and B, respectively, as shown in Figure 2.

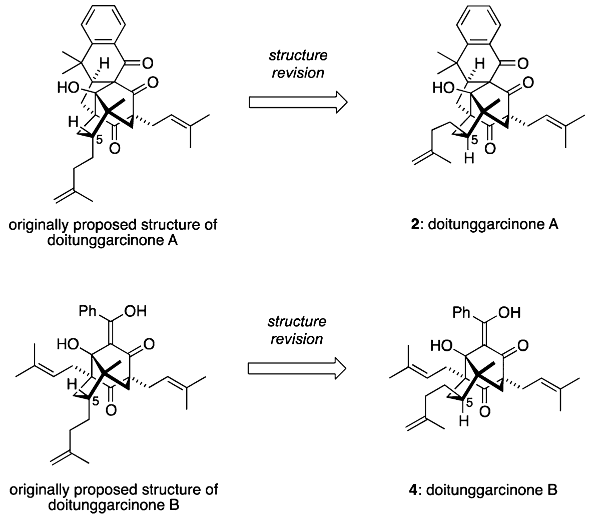
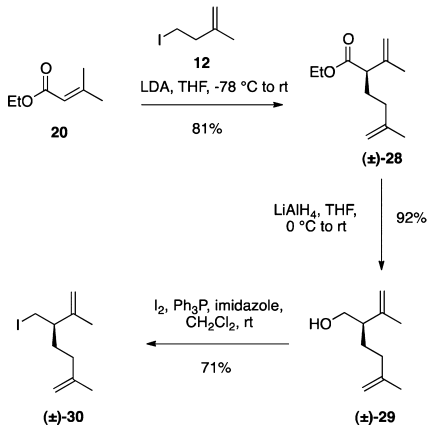


Figure 2. Suggested structure revision of doitunggarcinones A and B.

We sought to confirm our structural reassignment of doitunggarcinone A (**2**) through a total synthesis of the racemic compound. For this we first needed to synthesize alkyl iodide (±)-**30**, which was achieved according to Scheme 8.

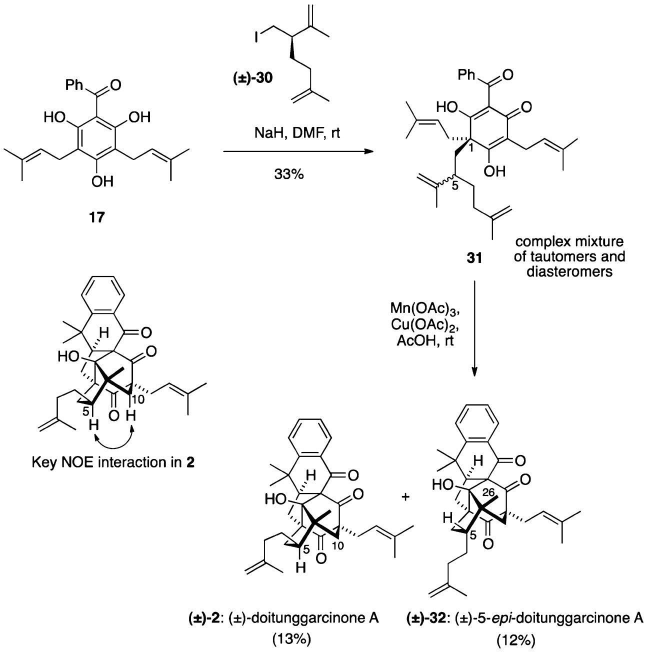
Scheme 8. Synthesis of Alkyl Iodide (±)-30



Alkylation of ethyl 3,3-dimethylacrylate (**20**) with 4-iodo-2-methyl-1-butene (**12**) and LDA gave (±)-**28**, which was reduced to give alcohol (±)-**29**. Iodination with I_2 and PPh_3 then gave (±)-**30** in good yield over the three steps. Unfortunately, an enantioselective synthesis of **30** following a similar strategy to that outlined in Scheme 6 proved elusive, as alkylation of (−)-**26** with 4-iodo-2-methyl-1-butene (**12**) was not possible.

Alkylative dearomatization of **17** with (±)-**30** formed **31** in 33% yield, and then oxidative cyclization gave (±)-doitunggarcinone A ((±)-**2**)) in 13% yield and (±)-5-*epi*-doitunggarcinone A ((±)-**32**)) in 12% yield (Scheme 9). NMR data for (±)-**2** fully matched the published data for the natural product. The relative configuration of (±)-**2** at C-5 was established via observation of a strong NOE between H-5 and H-10, thus

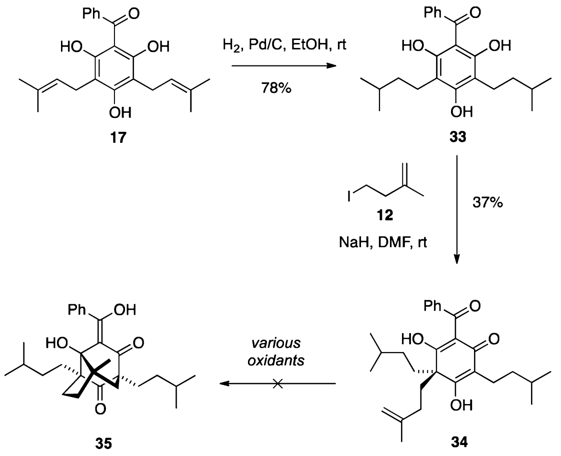
Scheme 9. Synthesis of (±)-Doitunggarcinone A



confirming our suggested structure revision. An NOE interaction between H-5 and Me-26 further confirmed the structure of (±)-**32**.

Interestingly, no formation of nemorosonol or doitunggarcinone B was ever observed in our total syntheses of garcibracteatone and doitunggarcinone A. Therefore, attempts were made to carry out a shortened radical cascade reaction with just two cyclization events that would allow synthesis of the nemorosonol/doitunggarcinone B ring system. Thus, deactivation of the prenyl side chains of **17** by hydrogenation gave **33** in 78% yield, which was then alkylated to give the dearomatized phloroglucinol **34** in 37% yield (Scheme 10). However, oxidation of **34** with a variety of oxidants gave complex mixtures of products, with no observed formation of the desired product **35**.

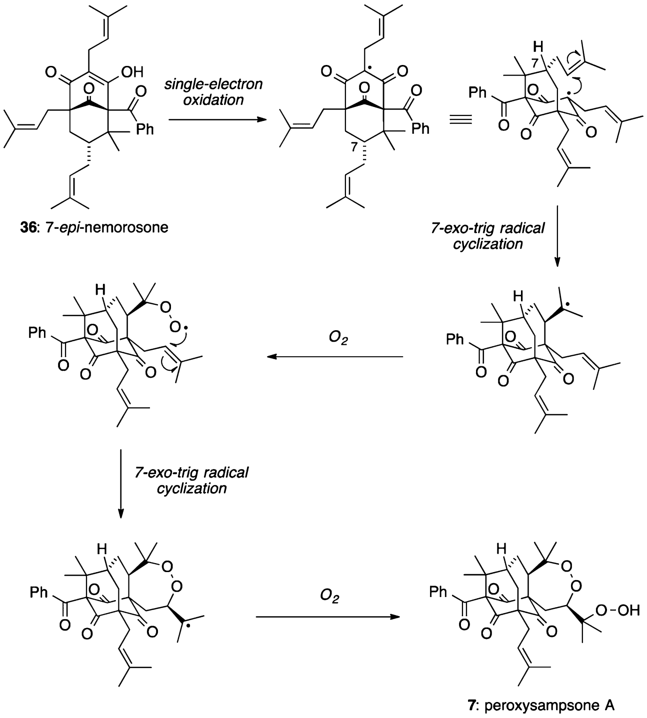
Scheme 10. Attempted Synthesis of the Nemorosonol/Doitunggarcinone B Ring System



CONCLUSION

We have shown that oxidative radical cyclizations are highly effective in the construction of complex PPAP natural products such as garcibracteatone (**1**) and doitunggarcinone A (**2**) and previously ialibinones A (**5**) and B (**6**). The success of these radical reactions in rapidly building up molecular complexity, with the formation of multiple stereocenters and carbon–carbon bonds in a single operation, perhaps indicates that similar pathways are involved in the biosynthesis of these PPAPs. Furthermore, we believe that there are several more PPAP natural products that could arise via complexity-generating radical cascade cyclizations. For example, the ornate structure of peroxysampsone A (**7**)[8] could be formed by oxidative radical cyclization of the related natural product 7-*epi*-nemorosone (**36**) according to Scheme 11. Initial single electron oxidation of **36** could give a stabilized α-diketo radical, which could undergo a 7-*exo-trig* radical cyclization onto the adjacent C-7 prenyl group to give a tertiary alkyl radical. Trapping of this radical with triplet oxygen, followed by 7-*exo-trig* cyclization of the resultant peroxyradical species, would then generate the complex ring system of peroxysampsone A (**7**).

Scheme 11. Proposed Biosynthesis of Peroxysampsone A



EXPERIMENTAL SECTION

General Methods. All chemicals used were purchased from commercial suppliers and used as received. All reactions were performed under an inert atmosphere of N_2. All organic extracts were dried over anhydrous magnesium sulfate. Thin layer chromatography was performed using aluminum sheets coated with silica gel. Visualization was aided by viewing under a UV lamp and staining with ceric ammonium molybdate stain followed by heating. All R_f values were measured to the nearest 0.01. Flash chromatography was performed using 40–63 μm grade silica gel. Melting points were recorded on a digital melting point apparatus and are uncorrected. Infrared spectra were recorded using an FT-IR spectrometer as the neat compounds. High field NMR was recorded using a 600 MHz spectrometer (^{1}H at 600 MHz, ^{13}C at 150 MHz). Solvents used for spectra were chloroform unless otherwise specified. ^{1}H chemical shifts are reported in ppm on the δ-scale relative to TMS (δ 0.0), and ^{13}C NMR are reported in ppm relative to chloroform (δ 77.0). Multiplicities are reported as (br) broad, (s) singlet, (d) doublet, (t) triplet, (q) quartet, and (m) multiplet. All J values were rounded to the nearest 0.1 Hz. ESI high resolution mass spectra were recorded on a Q-TOF mass spectrometer.

Phenyl(2,4,6-trihydroxyphenyl)methanone (10). To a suspension of anhydrous phloroglucinol (11.5 g, 91.2 mmol) in $PhNO_2$ (90 mL) was added $AlCl_3$ (48.6 g, 365 mmol) in three portions at rt. The reaction mixture was stirred at rt for 30 min. Benzoyl chloride (11.7 mL, 100 mmol) was added and was heated at 65 °C for 2 h. The reaction mixture was then cooled to rt before being quenched by pouring onto ice−water and extracted with EtOAc (3 × 100 mL). The product was then extracted into 2 M NaOH solution (2 × 150 mL). The aqueous extracts were neutralized with conc. HCl, and the product was extracted back into EtOAc (3 × 100 mL). The combined organics were washed sequentially with H_2O (100 mL) and brine (100 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by flash chromatography on SiO_2 (petrol/EtOAc, 4:1 → 2:1 gradient elution) to yield phenyl(2,4,6-trihydroxyphenyl)-methanone **10** (9.80 g, 47%) as a yellow solid. Data for **10**: R_f 0.10 (petrol/EtOAc, 2:1); mp 164−167 °C; IR (neat) 3363, 1638, 1594, 1286, 1151, 1056, 818, 697 cm^{-1}; ^{1}H NMR (600 MHz, acetone-d_6) δ 10.15 (br s, 3H), 7.57 (d, J = 7.2 Hz, 2H), 7.44 (t, J = 7.2 Hz, 1H), 7.36 (t, J = 7.2 Hz, 2H), 5.95 (s, 2H); ^{13}C NMR (150 MHz, acetone-d_6) δ 199.5, 165.2, 163.6, 142.3, 131.3, 128.6, 128.0, 104.9, 95.6.

(3,5-Diallyl-2,4,6-trihydroxyphenyl)(phenyl)methanone (11). To a solution of **10** (2.29 g, 9.95 mmol) in H_2O (20 mL), was added KOH (1.12 g, 19.9 mmol) at 0 °C. Allyl bromide (1.71 mL, 19.9 mmol) was then added dropwise over 20 min. The reaction mixture was warmed to rt and stirred for a further 1 h. The mixture was acidified with 1 M HCl solution (10 mL) and then extracted with EtOAc (3 × 20 mL). The combined organics were washed with brine (30 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by flash chromatography on SiO_2 (petrol/EtOAc, 8:1 as elutant) to give (3,5-diallyl-2,4,6-trihydroxyphenyl)(phenyl)methanone **11** (691 mg, 22%) as a yellow solid. Data for **11**: R_f 0.29 (petrol/EtOAc, 4:1); mp 83−85 °C; IR (neat) 3468, 3234, 2926, 1620, 1590, 1560, 1205, 1106, 911, 697 cm^{-1} ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.92 (s, 1H), 7.64 (dd, J = 8.2, 1.3 Hz, 2H), 7.59 (t, J = 7.5 Hz, 1H), 7.52 (t, J = 7.5 Hz, 2H), 5.98 (s, 1H), 6.00−5.92 (m, 2H), 5.15 (dq, J = 26.7, 1.6 Hz, 2H), 5.13 (dq, J = 19.6, 1.6 Hz, 2H), 3.41 (t, J = 1.6 Hz, 2H), 3.40 (t, J = 1.6 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 197.9, 161.0, 158.0, 139.9, 136.1, 132.2, 129.2, 127.8, 116.0, 104.6, 27.0; HRMS-ESI (m/z) calculated for $C_{19}H_{19}O_4$ [M + H]$^+$ 311.1278, found 311.1278.

4,6-Diallyl-2-benzoyl-3,5-dihydroxy-6-(3-methylbut-3-en-1-yl)cyclohexa-2,4-dienone (13). To a solution of **11** (400 mg, 1.29 mmol) in anhydrous DMF (8 mL) was added NaH (60% dispersion in mineral oil, 155 mg, 3.87 mmol) at rt. The mixture was stirred at rt for 5 min before 4-iodo-2-methyl-1-butene **12** (502 mg, 2.56 mmol) was added at rt. The reaction mixture was stirred at rt for 1 h. The mixture was quenched with 1 M HCl solution (10 mL) and extracted with EtOAc (3 × 15 mL). The combined organics were washed sequentially with H_2O (2 × 30 mL) and brine (30 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by flash chromatography on SiO_2 (petrol/EtOAc, 6:1 → 4:1 gradient elution) to give 4,6-diallyl-2-benzoyl-3,5-dihydroxy-6-(3-methylbut-3-en-1-yl)cyclohexa-2,4-dienone **13** (371 mg, 76%) as a yellow solid. Data for **13**: R_f 0.14 (petrol/EtOAc, 4:1); mp 97−101 °C; IR (neat) 3167, 2878, 1648, 1198, 890, 696 cm^{-1}; NMR spectra showed a complex mixture of tautomers; HRMS-ESI (m/z) calculated for $C_{24}H_{27}O_4$ [M + H]$^+$ 379.1904, found 379.1907.

7-Allyl-5a-benzoyl-2a1-hydroxy-8a-methyloctahydro-1*H*-2a,7-methanoacenaphthylene-6,9(2*H*)-dione (16). To a solution of $Mn(OAc)_3(H_2O)_2$ (212 mg, 0.79 mmol) in degassed EtOH (1 mL) was added **13** (150 mg, 0.396 mmol) in degassed EtOH (6 mL) at rt. The reaction mixture was stirred at rt for 3 h. The mixture was quenched with H_2O (15 mL) and was extracted with EtOAc (3 × 20 mL). The combined organics were washed sequentially with H_2O (30 mL) and brine (30 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by flash chromatography on SiO_2 (petrol/EtOAc, 10:1 as elutant) to give 7-allyl-5a-benzoyl-2a1-hydroxy-8a-methyloctahydro-1*H*-2a,7-methanoacenaphthylene-6,9(2*H*)-dione **16** (7 mg, 5%) as a white crystalline solid. Data for **16**: R_f 0.35 (petrol/EtOAc, 4:1); mp 115−117 °C; IR (neat) 3528, 2932, 1736, 1707, 1650, 1243, 1072, 914, 689 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.56 (dd, J = 8.2, 1.3 Hz, 2H), 7.52 (t, J = 7.5 Hz, 1H), 7.40 (t, J = 7.8 Hz, 2H), 5.71 (m, 1H), 5.09 (d, J = 4.1 Hz, 1H), 5.06 (s, 1H), 4.71 (s, 1H), 2.57 (dd, J = 14.4, 7.0 Hz, 1H), 2.39−2.30 (m, 2H), 2.28 (ddd, J = 12.7, 4.3, 2.2 Hz, 1H), 1.97 (m, 3H), 1.86 (td, J = 12.1, 6.7 Hz, 1H), 1.74 (ddd, J = 12.5, 9.5, 3.1 Hz, 1H), 1.58 (t, J = 7.1 Hz, 1H), 1.56−1.54 (m, 1H), 1.54−1.51 (m, 1H), 1.43 (ddd, J = 13.5, 9.5, 6.7 Hz, 1H), 1.18 (s, 3H), 0.95−0.82 (m, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 210.8, 207.2, 204.6, 137.9, 133.4, 132.1, 128.3, 127.9, 118.7, 80.6, 66.5, 65.7, 62.8, 43.3, 40.5, 39.0, 35.5, 31.3, 30.6, 28.0, 23.3, 19.8; HRMS-ESI (m/z) calculated for $C_{24}H_{27}O_4$ [M + H]$^+$ 379.1904, found 379.1901.

Phenyl(2,4,6-trihydroxy-3,5-bis(3-methylbut-2-en-1-yl)-phenyl)methanone (17). To a solution of **10** (10.0 g, 43.4 mmol) in H_2O (80 mL) was added KOH (4.89 g, 86.9 mmol) at 0 °C. Prenyl bromide (10.0 mL, 86.9 mmol) was then added dropwise over 20 min at 0 °C. The reaction mixture was stirred at 0 °C for a further 1 h. The reaction mixture was acidified with 1 M HCl solution (40 mL) and then extracted with EtOAc (3 × 100 mL). The combined organics were washed with brine (200 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by flash chromatography on SiO_2 (petrol/EtOAc, 20:1 → 10:1 gradient elution) to give phenyl(2,4,6-trihydroxy-3,5-bis(3-methylbut-2-en-1-yl)phenyl)-methanone **17** (5.35 g, 34%) as a yellow solid. Data for **17**: R_f 0.45 (petrol/EtOAc, 4:1); mp 76−82 °C; IR (neat) 3360, 2912, 1618, 1560, 1427, 1325, 1098, 694 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.91 (s, 2H), 7.65−7.62 (m, 2H), 7.59−7.55 (m, 1H), 7.52−7.48 (m, 2H), 6.35 (s, 1H), 5.22 (t, J = 7.1 Hz, 2H), 3.34 (d, J = 7.0 Hz, 4H), 1.78 (s, 6H), 1.74 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 198.0, 161.0, 157.6, 140.3, 135.0, 132.0, 129.0, 127.9, 121.8, 106.3, 104.5, 25.8, 21.8, 17.9.

2-Benzoyl-3,5-dihydroxy-4,6-bis(3-methylbut-2-en-1-yl)-6-(3-methylbut-3-en-1-yl)cyclohexa-2,4-dienone (18). To a solution of **17** (454 mg, 1.24 mmol) in anhydrous DMF (5 mL) was added NaH (60% dispersion in mineral oil, 149 mg, 3.72 mmol) at rt. The mixture was stirred at rt for 5 min. 4-Iodo-2-methyl-1-butene **12** (0.29 mL, 2.48 mmol) was then added at rt. The reaction mixture was stirred at rt for 1 h. The mixture was quenched with 1 M HCl solution (10 mL) and extracted with EtOAc (3 × 15 mL). The combined organics were washed sequentially with H_2O (2 × 30 mL) and brine (30 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by flash chromatography on SiO_2 (petrol/EtOAc, 6:1 → 4:1 gradient elution) to give 2-benzoyl-3,5-dihydroxy-4,6-bis(3-methylbut-2-en-1-yl)-6-(3-methylbut-3-en-1-yl)-cyclohexa-2,4-dienone **18** (293 mg, 54%) as a viscous yellow oil. Data for **18**: R_f 0.23 (petrol/EtOAc, 4:1); IR (neat) 2914, 1647, 1446, 1370, 1186, 693 cm^{-1}; NMR spectra showed a complex mixture of tautomers; HRMS-ESI (m/z) calculated for $C_{28}H_{35}O_4$ [M + H]$^+$ 435.2530, found 435.2528.

2a1-Hydroxy-4,4,12a-trimethyl-11-(3-methylbut-2-en-1-yl)-3,3a,4,11,12,12a-hexahydro-1*H*-2a,11-methanocyclopenta-[3,4]indeno[1,7a-*b*]naphthalene-9,10,13(2*H*,2a1*H*)-trione (19). To a solution of $Mn(OAc)_3(H_2O)_2$ (252 mg, 0.94 mmol) and $Cu(OAc)_2(H_2O)$ (86 mg, 0.45 mmol) in degassed AcOH (2 mL) was added **18** (195 mg, 0.45 mmol) in degassed AcOH (8 mL) at rt. The reaction mixture was stirred at rt for 3 h. The mixture was quenched with H_2O (15 mL) and extracted with EtOAc (3 × 20 mL). The combined organics were washed sequentially with H_2O (30 mL), sat. $NaHCO_3$ solution (30 mL) and brine (30 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by flash chromatography on SiO_2 (petrol/EtOAc, 10:1 as elutant) to give 2a1-hydroxy-4,4,12a-trimethyl-11-(3-methylbut-2-en-1-yl)-3,3a,4,11,12,12a-hexahydro-1*H*-2a,11 methanocyclopenta[3,4]indeno-[1,7a-*b*]naphthalene-9,10,13(2*H*,2a1*H*)-trione **19** (50 mg, 25%) as a white crystalline solid. Data for **19**: R_f 0.42 (petrol/EtOAc, 4:1); mp 204−206 °C; IR (neat) 3468, 2949, 1736, 1707, 1663, 1599, 1118, 765 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.70 (dd, *J* = 7.6, 1.3 Hz 1H), 7.54 (td, *J* = 7.6, 1.3 Hz, 1H), 7.36 (t, *J* = 7.6 Hz, 1H), 7.35 (d, *J* = 7.6 Hz, 1H), 5.05 (t, *J* = 7.2 Hz, 1H), 2.85 (s, 1H), 2.68 (dd, *J* = 9.8, 7.7 Hz, 1H), 2.37 (t, *J* = 12.1 Hz, 1H), 2.28 (d, *J* = 7.3 Hz, 2H), 2.26−2.23 (m, 1H), 2.06 (dd, *J* = 11.5, 7.7 Hz, 1H), 1.98−1.93 (m, 1H), 1.82−1.71 (m, 2H), 1.78 (d, *J* = 13.9 Hz, 1H), 1.68 (d, *J* = 13.9 Hz, 1H), 1.65 (s, 3H), 1.57 (s, 3H), 1.49 (s, 3H), 1.36 (s, 3H), 1.11 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 213.4, 203.4, 200.2, 150.3, 136.3, 134.3, 133.7, 126.9, 126.4, 123.5, 118.8, 90.9, 72.8, 68.5, 63.1, 57.0, 46.0, 44.7, 39.5, 37.2, 29.9, 29.0, 26.2, 25.9, 25.1, 24.5, 22.9, 17.9; HRMS-ESI (*m*/*z*) calculated for $C_{28}H_{33}O_4$ [M + H]$^+$ 433.2373, found 433.2372.

(±)-Ethyl 5-methyl-2-(prop-1-en-2-yl)hex-4-enoate ((±)-21). To a solution of LDA (2.0 M in heptane, 46.8 mL, 93.6 mmol) and anhydrous THF (80 mL) was added ethyl 3,3-dimethyl acrylate **20** (10.0 g, 78 mmol) in anhydrous THF (12 mL) dropwise at −78 °C. The mixture was stirred at −78 °C for 15 min. Prenyl bromide (9.90 mL, 85.8 mmol) was then added at −78 °C. The reaction mixture was stirred for a further 1 h before gradual warming to rt. The mixture was quenched with satd NH_4Cl solution (100 mL) and extracted with Et_2O (3 × 100 mL). The combined organics were washed with brine (200 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by flash chromatography on SiO_2 (petrol/EtOAc, 20:1 as elutant) to give (±)-ethyl 5-methyl-2-(prop-1-en-2-yl)hex-4-enoate (±)-**21** (13.3 g, 87%) as a colorless oil. Data for (±)-**21**: R_f 0.65 (petrol/EtOAc, 4:1); IR (neat) 2976, 1733, 1647, 1179, 1150, 895 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.03 (t, *J* = 7.1 Hz, 1H), 4.91−4.86 (m, 2H), 4.13 (qd, *J* = 7.1, 1.8 Hz, 2H), 3.01 (t, *J* = 7.7 Hz, 1H), 2.51 (dt, *J* = 15.1, 7.8 Hz, 1H), 2.26 (dt, *J* = 14.3, 7.0 Hz, 1H), 1.76 (s, 3H), 1.68 (s, 3H), 1.62 (d, *J* = 11.5 Hz, 3H), 1.24 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.5, 142.5, 133.4, 121.2, 113.4, 60.4, 53.3, 29.0, 25.7, 20.5, 17.8, 14.2.

(±)-5-Methyl-2-(prop-1-en-2-yl)hex-4-en-1-ol ((±)-22). To a solution of $LiAlH_4$ (5.60 g, 148 mmol) in Et_2O (200 mL) was added **21** (13.2 g, 67.5 mmol) in Et_2O (60 mL) dropwise over 20 min at 0 °C. The reaction mixture was warmed to rt and stirred for 1 h. The mixture was then cooled to 0 °C, quenched by careful dropwise addition of H_2O (5.6 mL), and stirred at rt for 5 min. Then 15% NaOH solution (5.6 mL) was added, and the mixture was stirred at rt for a further 5 min before H_2O (16.8 mL) was added. The mixture was filtered and extracted thoroughly with Et_2O, and the filtrate was concentrated *in vacuo* to yield (±)-5-methyl-2-(prop-1-en-2-yl)hex-4-en-1-ol (±)-**22** (9.90 g, 95%) as a colorless oil which was used in the next step without further purification. Data for (±)-**22**: R_f 0.39 (petrol/EtOAc, 4:1); IR (neat) 3351, 2916, 1646, 1440, 1376, 1038, 888 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.08 (tt, *J* = 7.2, 1.2 Hz, 1H), 4.94−4.91 (m, 1H), 4.82 (d, *J* = 0.6 Hz, 1H), 3.57 (dt, *J* = 11.3, 5.8 Hz, 1H), 3.50 (dt, *J* = 8.7, 3 Hz, 1H) 2.28 (qd, *J* = 7.6, 5.2 Hz, 1H), 2.11 (dt, *J* = 14.6, 7.3 Hz, 1H), 2.04 (dt, *J* = 14.6, 7.1 Hz, 1H), 1.70 (s, 3H), 1.69 (s, 3H), 1.61 (s, 3H), 1.43 (t, *J* = 5.3 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 145.4, 132.7, 122.0, 113.1, 63.6, 49.9, 28.4, 25.7, 19.5, 17.8.

(±)-3-(Iodomethyl)-2,6-dimethylhepta-1,5-diene ((±)-23). To a solution of PPh_3 (18.5 g, 70.6 mmol) and imidazole (4.80 g, 70.6 mmol) in CH_2Cl_2 (200 mL) was added I_2 (17.9 g, 70.6 mmol) at 0 °C. The mixture was stirred at 0 °C for 15 min. Then **22** (9.90 mL, 64.2 mmol) in CH_2Cl_2 (30 mL) was added dropwise at 0 °C. The reaction mixture was stirred at rt for 2 h. The mixture was quenched with $Na_2S_2O_3$ solution (36 g in 200 mL of H_2O) and stirred at rt for 10 min. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (200 mL). The combined organics were washed with brine (200 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by flash chromatography on SiO_2 (neat petrol as elutant) to give (±)-3-(iodomethyl)-2,6-dimethylhepta-1,5-diene (±)-**23** (14,6 g, 86%) as a pale orange oil. Data for (±)-**23**: R_f 0.70 (neat petrol); IR (neat) 2968, 2913, 1647, 1439, 1375, 1187, 893 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.03 (tt, *J* = 7.9, 1.3 Hz, 1H), 4.91−4.89 (m, 1H), 4.75 (s, 1H), 3.28 (dd, *J* = 9.8, 5.8 Hz, 1H), 3.19 (dd, *J* = 9.8, 7.7 Hz, 1H), 2.29 (dt, *J* = 14.3, 7.1, 1H), 2.24 (dt, *J* = 14.3, 7.1 Hz, 1H), 2.11 (dt, *J* = 14.3, 7.0 Hz, 1H), 1.69 (s, 3H), 1.68 (s, 3H), 1.63 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 145.5, 133.4, 121.5, 112.8, 49.4, 39.9, 25.8, 19.3, 18.0, 11.3.

(±)-2-Benzoyl-3,5-dihydroxy-6-(5-methyl-2-(prop-1-en-2-yl)hex-4-en-1-yl)-4,6-bis(3-methylbut-2-en-1-yl)cyclohexa-2,4-dienone ((±)-24). To a solution of **17** (616 mg, 1.68 mmol) in anhydrous DMF (12 mL) was added NaH (242 mg, 10.1 mmol) at rt. The mixture was stirred at rt for 10 min. Iodide (±)-**23** (2.66 g, 10.1 mmol) in anhydrous DMF (2 mL) was then added at rt. The reaction mixture was stirred at rt for 1 h. The mixture was quenched with 1 M HCl solution (15 mL) and extracted with EtOAc (3 × 20 mL). The combined organics were washed sequentially with H_2O (2 × 30 mL) and brine (30 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by flash chromatography on SiO_2 (petrol/EtOAc, 50:1 → 15:1 gradient elution) to give (±)-2-benzoyl-3,5-dihydroxy-6-(5-methyl-2-(prop-1-en-2-yl)hex-4-en-1-yl)-4,6-bis(3-methylbut-2-en-1-yl)cyclohexa-2,4-dienone (±)-**24** (242 mg, 29%, 50% BRSM) as a viscous yellow oil. Data for (±)-**24**: R_f 0.42 (petrol/EtOAc, 4:1); IR (neat) 3278, 2914, 1645, 1445, 1182, 695 cm^{-1}; NMR showed a complex mixture of tautomers and diasteroisomers; HRMS-ESI (*m*/*z*) calculated for $C_{33}H_{43}O_4$ [M + H]$^+$ 503.3156, found 503.3149.

(±)-Garcibracteatone (1) and (±)-5-*epi*-Garcibracteatone (25). To a solution of $Mn(OAc)_3(H_2O)_2$ (457 mg, 1.70 mmol) and $Cu(OAc)_2(H_2O)$ (154 mg, 0.85 mmol) in degassed AcOH (2 mL) was added (±)-**24** (408 mg, 0.81 mmol) in degassed AcOH (12 mL) at rt. The reaction mixture was stirred at rt for 3 h. The mixture was quenched with H_2O (20 mL) and extracted with EtOAc (3 × 30 mL). The combined organics were washed sequentially with H_2O (50 mL), sat. $NaHCO_3$ solution (50 mL), and brine (50 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by flash chromatography on SiO_2 (petrol/EtOAc, 20:1 → 15:1 gradient elution) to give (±)-garcibracteatone (±)-**1** (56 mg, 14%) as a white crystalline solid. Data for (±)-**1**: R_f 0.62 (petrol/EtOAc, 4:1); mp 196−199 °C; IR (neat) cm^{-1} 3468, 2977, 1736, 1706, 1665, 1601, 1450, 1260, 1111, 765; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.69 (dd, *J* = 7.6, 1.3 Hz, 1H), 7.54 (td, *J* = 7.6, 1.4 Hz, 1H), 7.36 (t, *J* = 7.6 Hz, 1H), 7.35 (d, *J* = 7.6 Hz, 1H), 5.04 (t, *J* = 7.2 Hz, 1H), 5.01 (t, *J* = 7.2 Hz, 1H), 2.83 (s, 1H), 2.66 (dd, *J* = 9.9, 7.8 Hz, 1H), 2.30−2.23 (m, 1H), 2.27 (d, *J* = 7.3 Hz, 1H), 2.20 (dd, *J* = 11.3, 10.1 Hz, 1H), 2.12−2.05 (m, 1H), 2.07 (dd, *J* = 11.5, 7.8 Hz, 1H), 2.01 (dd, *J* = 11.8, 7.9 Hz, 1H), 1.89−1.82 (m, 1H), 1.77 (d, *J* = 13.9 Hz, 1H), 1.68 (d, *J* = 13.8 Hz, 1H), 1.68 (s, 3H), 1.65 (s, 3H), 1.62 (s, 3H), 1.59−1.55 (m, 1H), 1.57 (s, 3H), 1.55 (s, 1H), 1.46 (s, 3H), 1.35 (s, 3H), 1.10 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 213.3, 203.3, 200.3, 150.2, 136.4, 134.3, 133.6, 132.4, 126.9, 126.4, 123.5, 122.9, 118.8, 91.8, 70.2, 69.2, 63.2, 56.9, 56.8, 47.5, 41.5, 37.1, 33.0, 32.5, 29.8, 29.0, 26.2, 25.9, 25.8, 25.1, 18.4, 18.0, 17.9; HRMS-ESI (*m*/*z*) calculated for $C_{33}H_{41}O_4$ [M + H]$^+$ 501.2999, found 501.3002. Further elution gave (±)-5-*epi*-garcibracteatone (±)-**25** (31 mg, 8%) as a white crystalline solid. Data for **25**: R_f 0.58 (petrol/EtOAc, 4:1); mp 212−216 °C; IR (neat) 3487, 2964, 1735, 1706, 1666, 1598, 1455, 1298, 1107, 760 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.70 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.54 (td, *J* = 7.6, 1.4 Hz, 1H), 7.36 (t, *J* = 7.6 Hz, 1H), 7.35 (d, *J* = 7.8 Hz, 1H), 5.11 (t, *J* = 7.3 Hz, 1H), 5.02 (t, *J* = 6.9 Hz, 1H), 2.81 (s, 1H), 2.62 (dd, *J* = 9.8, 7.7 Hz, 1H), 2.53−2.47 (m, 1H), 2.33−2.26 (m, 1H), 2.29 (d, *J* = 8.0 Hz, 1H), 2.20 (dd, *J* = 11.2, 10.1 Hz, 1H), 2.12 (dd, *J* = 12.3, 10.9 Hz, 1H), 2.05 (t, *J* = 9.5 Hz, 1H), 2.03 (d, *J* = 14.2 Hz, 1H), 1.93−1.87 (m, 1H), 1.72−1.65 (m, 1H), 1.69 (s, 3H), 1.66 (s, 3H), 1.58 (s, 3H), 1.58 (s, 3H), 1.47 (s, 3H), 1.43 (d, *J* = 14.5 Hz, 1H), 1.38−1.34 (m, 1H), 1.35 (s, 3H), 1.10 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 213.4, 203.3, 200.2, 150.2, 136.3, 134.6, 133.7, 132.6, 126.9, 126.4, 123.5, 122.8, 119.0, 91.8, 71.0, 69.1, 63.0, 56.2, 52.5, 42.5, 37.2, 35.1, 31.1, 30.2, 29.8, 29.5, 26.2, 25.9, 25.8, 24.8, 22.8, 17.9, 17.8; HRMS-ESI (*m*/*z*) calculated for $C_{33}H_{41}O_4$ [M + H]$^+$ 501.2999, found 501.3018.

(*S*)-4-Benzyl-3-((*S*)-5-methyl-2-(prop-1-en-2-yl)hex-4-enoyl)-oxazolidin-2-one ((+)-27). To a solution of (−)-**26** (9.31 g, 35.9 mmol) in THF (100 mL) was added NaHMDS (1.0 M solution in THF, 39.5 mL, 39.5 mmol) at −78 °C. The mixture was stirred at −78 °C for 1 h before addition of prenyl bromide (8.30 mL, 71.8 mmol) dropwise at −78 °C. The resultant mixture was stirred at −78 °C for 6 h. The mixture was quenched with satd NH_4Cl solution (100 mL) and extracted with Et_2O (3 × 100 mL). The combined organics were washed with brine (100 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by flash chromatography on SiO_2 (petrol/EtOAc, 10:1 as elutant) to give (*S*)-4-benzyl-3-((*S*)-5-methyl-2-(prop-1-en-2-yl)hex-4-enoyl)-oxazolidin-2-one (+)-**27** (7.78 g, 66%) as a colorless oil. Data for (+)-**27**: 0.40 (petrol/EtOAc, 4:1); IR (neat) 2919, 1775, 1697, 1206, 701 cm^{-1}; $[\alpha]^{25}_{D}$ (*c* 1.0, $CHCl_3$) +102.6°; ^1H NMR (600 MHz, $CDCl_3$) δ 7.33 (t, *J* = 7.3 Hz, 2H), 7.29−7.25 (m, 1H), 7.21 (d, *J* = 7.0 Hz, 2H), 5.14 (t, *J* = 7.2 Hz, 1H), 4.89 (d, *J* = 7.7 Hz, 2H), 4.69−4.63 (m, 1H), 4.47 (dd, *J* = 9.0, 5.8 Hz, 1H), 4.17−4.11 (m, 2H), 3.22 (dd, *J* = 13.4, 3.3 Hz, 1H), 2.78 (dd, *J* = 13.5, 9.3 Hz, 1H), 2.62 (dt, *J* = 15.8, 8.3 Hz, 1H), 2.36−2.29 (m, 1H), 1.83 (s, 3H), 1.70 (s, 3H), 1.67 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.3, 153.0, 143.1, 135.3, 133.8, 129.4, 128.9, 127.3, 121.4, 113.4, 65.7, 55.5, 50.3, 37.8, 29.8, 25.8, 21.3, 17.8; HRMS-ESI (*m*/*z*) calculated for $C_{20}H_{26}NO_3$ $[M + H]^+$ 328.1907 found 328.1907.

(*S*)-5-Methyl-2-(prop-1-en-2-yl)hex-4-en-1-ol ((−)-22). To a solution of (+)-**27** (3.26 g, 9.98 mmol) in Et_2O (30 mL) and MeOH (0.53 mL, 12.9 mmol) was added $LiBH_4$ (283 mg, 12.9 mmol) at 0 °C. The resultant mixture was stirred at rt for 1 h. The mixture was quenched with satd NH_4Cl solution (50 mL) and extracted with Et_2O (3 × 50 mL). The combined organics were washed with brine (100 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by flash chromatography on SiO_2 (petrol/EtOAc, 6:1 as elutant) to give (*S*)-3-(iodomethyl)-2,6-dimethylhepta-1,5-diene (−)-**22** (975 mg, 63%) as a colorless oil. Data for (−)-**22**: R_f 0.40 (petrol/EtOAc, 4:1); IR (neat) 3351, 2916, 1646, 1440, 1376, 1038, 888 cm^{-1}; $[\alpha]^{25}_{D}$ (*c* 1.0, $CHCl_3$) −2.0; ^1H NMR (600 MHz, $CDCl_3$) δ 5.08 (tt, *J* = 7.2, 1.2 Hz, 1H), 4.94−4.91 (m, 1H), 4.82 (d, *J* = 0.6 Hz, 1H), 3.57 (dt, *J* = 11.3, 5.8 Hz, 1H), 3.50 (dt, *J* = 8.7, 3 Hz, 1H) 2.28 (qd, *J* = 7.6, 5.2 Hz, 1H), 2.11 (dt, *J* = 14.6, 7.3 Hz, 1H), 2.04 (dt, *J* = 14.6, 7.1 Hz, 1H), 1.70 (s, 3H), 1.69 (s, 3H), 1.61 (s, 3H), 1.43 (t, *J* = 5.3 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 145.4, 132.7, 122.0, 113.1, 63.6, 49.9, 28.4, 25.7, 19.5, 17.8.

(*S*)-3-(Iodomethyl)-2,6-dimethylhepta-1,5-diene ((−)-23). To a solution of PPh_3 (3.68 g, 14.0 mmol) and imidazole (954 mg, 14.0 mmol) in CH_2Cl_2 (70 mL) was added I_2 (3.56 g, 1.40 mmol) at 0 °C. The mixture was stirred at 0 °C for 15 min. (−)-**22** (2.06 mL, 13.4 mmol) in CH_2Cl_2 (10 mL) was then added dropwise at 0 °C. The reaction mixture was stirred at rt for 2 h. The mixture was quenched with $Na_2S_2O_3$ solution (18 g in 100 mL of H_2O) and stirred at rt for 10 min. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (100 mL). The combined organics were washed with brine (100 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by flash chromatography on SiO_2 (neat petrol as elutant) to give (*S*)-3-(iodomethyl)-2,6-dimethylhepta-1,5-diene (−)-**23** (2.70 g, 77%) as a pale orange oil. Data for (−)-**23**: R_f 0.70 (neat petrol); IR (neat) 2968, 2913, 1647, 1439, 1375, 1187, 893 cm^{-1}; $[\alpha]^{25}_{D}$ (*c* 1.0, $CHCl_3$) −1.8; ^1H NMR (600 MHz, $CDCl_3$) δ 5.03 (tt, *J* = 7.9, 1.3 Hz, 1H), 4.91−4.89 (m, 1H), 4.75 (s, 1H), 3.28 (dd, *J* = 9.8, 5.8 Hz, 1H), 3.19 (dd, *J* = 9.8, 7.7 Hz, 1H), 2.29 (dt, *J* = 14.3, 7.1, 1H), 2.24 (dt, *J* = 14.3, 7.1 Hz, 1H), 2.11 (dt, *J* = 14.3, 7.0 Hz, 1H), 1.69 (s, 3H), 1.68 (s, 3H), 1.63 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 145.5, 133.4, 121.5, 112.8, 49.4, 39.9, 25.8, 19.3, 18.0, 11.3.

(−)-4-Benzoyl-5-hydroxy-6-((*R*)-5-methyl-2-(prop-1-en-2-yl)-hex-4-en-1-yl)-2,6-bis(3-methylbut-2-en-1-yl)cyclohex-4-ene-1,3-dione ((−)-24). To a solution of **17** (620 mg, 1.70 mmol) in anhydrous DMF (12 mL) was added NaH (164 mg, 10.2 mmol) at rt. The mixture was stirred at rt for 10 min. Iodide (−)-**23** (2.70 g, 10.2 mmol) in anhydrous DMF (2 mL) was then added at rt. The reaction mixture was stirred at rt for 1 h. The mixture was quenched with 1 M HCl solution (15 mL) and extracted with EtOAc (3 × 20 mL). The combined organics were washed sequentially with H_2O (2 × 30 mL) and brine (30 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by flash chromatography on SiO_2 (petrol/EtOAc, 50:1 → 15:1 gradient elution) to give (−)-4-benzoyl-5-hydroxy-6-((*R*)-5-methyl-2-(prop-1-en-2-yl)hex-4-en-1-yl)-2,6-bis(3-methylbut-2-en-1-yl)cyclohex-4-ene-1,3-dione (−)-**24** (252 mg, 29%, 50% BRSM) as a viscous yellow oil. Data for (−)-**24**: R_f 0.42 (petrol/EtOAc, 4:1); IR (neat) 3278, 2914, 1645, 1445, 1182, 695 cm^{-1}; $[\alpha]^{25}_{D}$ (*c* 1.0, $CHCl_3$) −7.8; NMR showed a complex mixture of tautomers and diasteroisomers; HRMS-ESI (*m*/*z*) calculated for $C_{33}H_{43}O_4$ $[M + H]^+$ 503.3156, found 503.3149.

(+)-Garcibracteatone (1) and (−)-5-*epi*-Garcibracteatone (25). To a solution of $Mn(OAc)_3(H_2O)_2$ (280 mg, 1.04 mmol) and $Cu(OAc)_2(H_2O)$ (95 mg, 0.497 mmol) in degassed AcOH (2 mL) was added **24** (250 mg, 0.497 mmol) in degassed AcOH (8 mL) at rt. The reaction mixture was stirred at rt for 3 h. The mixture was quenched with H_2O (15 mL) and was extracted with EtOAc (3 × 20 mL). The combined organics were washed sequentially with H_2O (30 mL), satd $NaHCO_3$ solution (30 mL), and brine (30 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by flash chromatography on SiO_2 (petrol/EtOAc, 20:1 → 15:1 gradient elution) to give (+)-garcibracteatone (+)-**1** (36 mg, 14%) as a white crystalline solid. Data for **1**: R_f 0.62 (petrol/EtOAc, 4:1); mp 196−199 °C; IR (neat) cm^{-1} 3468, 2977, 1736, 1706, 1665, 1601, 1450, 1260, 1111, 765; $[\alpha]^{25}_{D}$ (*c* 1.0, $CHCl_3$) +2.0; ^1H NMR (600 MHz, $CDCl_3$) δ 7.69 (dd, *J* = 7.6, 1.3 Hz, 1H), 7.54 (td, *J* = 7.6, 1.4 Hz, 1H), 7.36 (t, *J* = 7.6 Hz, 1H), 7.35 (d, *J* = 7.6 Hz, 1H), 5.04 (t, *J* = 7.2 Hz, 1H), 5.01 (t, *J* = 7.2 Hz, 1H), 2.83 (s, 1H), 2.66 (dd, *J* = 9.9, 7.8 Hz, 1H), 2.30−2.23 (m, 1H), 2.27 (d, *J* = 7.3 Hz, 1H), 2.20 (dd, *J* = 11.3, 10.1 Hz, 1H), 2.12 −2.05 (m, 1H), 2.07 (dd, *J* = 11.5, 7.8 Hz, 1H), 2.01 (dd, *J* = 11.8, 7.9 Hz, 1H), 1.89−1.82 (m, 1H), 1.77 (d, *J* = 13.9 Hz, 1H), 1.68 (d, *J* = 13.8 Hz, 1H), 1.68 (s, 3H), 1.65 (s, 3H), 1.62 (s, 3H), 1.59−1.55 (m, 1H), 1.57 (s, 3H), 1.55 (s, 1H), 1.46 (s, 3H), 1.35 (s, 3H), 1.10 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 213.3, 203.3, 200.3, 150.2, 136.4, 134.3, 133.6, 132.4, 126.9, 126.4, 123.5, 122.9, 118.8, 91.8, 70.2, 69.2, 63.2, 56.9, 56.8, 47.5, 41.5, 37.1, 33.0, 32.5, 29.8, 29.0, 26.2, 25.9, 25.8, 25.1, 18.4, 18.0, 17.9; HRMS-ESI (*m*/*z*) calculated for $C_{33}H_{41}O_4$ $[M + H]^+$ 501.2999, found 501.3002. Further elution gave (−)-5-*epi*-garcibracteatone (−)-**25** (21 mg, 8%) as a white crystalline solid. Data for **25**: R_f 0.58 (petrol/EtOAc, 4:1); mp 212−216 °C; IR (neat) 3487, 2964, 1735, 1706, 1666, 1598, 1455, 1298, 1107, 760 cm^{-1}; $[\alpha]^{25}_{D}$ (*c* 1.0, $CHCl_3$) −34.1; ^1H NMR (600 MHz, $CDCl_3$) δ 7.70 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.54 (td, *J* = 7.6, 1.4 Hz, 1H), 7.36 (t, *J* = 7.6 Hz, 1H), 7.35 (d, *J* = 7.8 Hz, 1H), 5.11 (t, *J* = 7.3 Hz, 1H), 5.02 (t, *J* = 6.9 Hz, 1H), 2.81 (s, 1H), 2.62 (dd, *J* = 9.8, 7.7 Hz, 1H), 2.53−2.47 (m, 1H), 2.33−2.26 (m, 1H), 2.29 (d, *J* = 8.0 Hz, 1H), 2.20 (dd, *J* = 11.2, 10.1 Hz, 1H), 2.12 (dd, *J* = 12.3, 10.9 Hz, 1H), 2.05 (t, *J* = 9.5 Hz, 1H), 2.03 (d, *J* = 14.2 Hz, 1H), 1.93−1.87 (m, 1H), 1.72−1.65 (m, 1H), 1.69 (s, 3H), 1.66 (s, 3H), 1.58 (s, 3H), 1.58 (s, 3H), 1.47 (s, 3H), 1.43 (d, *J* = 14.5 Hz, 1H), 1.38−1.34 (m, 1H), 1.35 (s, 3H), 1.10 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 213.4, 203.3, 200.2, 150.2, 136.3, 134.6, 133.7, 132.6, 126.9, 126.4, 123.5, 122.8, 119.0, 91.8, 71.0, 69.1, 63.0, 56.2, 52.5, 42.5, 37.2, 35.1, 31.1, 30.2, 29.8, 29.5, 26.2, 25.9, 25.8, 24.8, 22.8, 17.9, 17.8; HRMS-ESI (*m*/*z*) calculated for $C_{33}H_{41}O_4$ $[M + H]^+$ 501.2999, found 501.3018.

(±)-Ethyl 5-Methyl-2-(prop-1-en-2-yl)hex-5-enoate ((±)-28). To a solution of fresh LDA prepared *in situ* from iPr_2NH (4.64 mL, 33.1 mmol) and *n*-BuLi (13.2 mL, 2.5 M in hexanes, 33.1 mmol) in THF (50 mL) was added ethyl 3,3-dimethyl acrylate **20** (2.29 mL, 16.5 mmol) dropwise at −78 °C. The reaction mixture was stirred for 30 min, then 4-iodo-2-methyl-1-butene **12** (4.86 g, 24.8 mmol) was added dropwise, and the mixture stirred for 30 min, then warmed to 0 °C, and stirred for a further 2 h. The reaction was quenched with satd NH_4Cl (50 mL), the product was extracted with EtOAc (3 × 100 mL), and the combined organics washed with H_2O (300 mL) and brine (300 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo* to give (±)-ethyl 5-methyl-2-(prop-1-en-2-yl)hex-5-enoate (±)-**28** (2.61 g, 81%) as an orange-yellow oil which was used in the next step without further purification. Data for (±)-**28**: R_f 0.60 (petrol/EtOAc, 4:1); IR(neat) 2933, 1731, 1648, 1447, 1374, 1151, 1030, 890 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.90 (s, 1H), 4.89 (s, 1H), 4.73 (s, 1H), 4.69 (s, 1H), 4.14 (q, J = 7.1 Hz, 2H), 3.11−2.94 (m, 1H), 2.04−1.91 (m, 2H), 1.75 (s, 3H), 1.72 (s, 3H), 1.76−1.67 (m, 2H), 1.25 (t, J = 7.1 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.6, 145.0, 142.4, 113.8, 110.5, 60.5, 52.5, 35.4, 28.0, 22.3, 20.2, 14.2; HRMS-ESI (*m/z*) calculated for $C_{12}H_{21}O_2$ $[M + H]^+$ 197.1536, found 197.1534.

(±)-5-Methyl-2-(prop-1-en-2-yl)hex-5-en-1-ol ((±)-29). To a solution of $LiAlH_4$ (1.11 g, 29.3 mmol) in Et_2O (35 mL) at 0 °C was added a solution of (±)-**28** (2.61 g, 13.3 mmol) in Et_2O (20 mL) dropwise over 10 min. The reaction mixture was warmed to rt and stirred for 1 h and then quenched carefully with successive addition of H_2O (1.11 mL), 15% NaOH (1.11 mL), and H_2O (3.33 mL). The product was extracted with EtOAc (2 × 30 mL), the undesired precipitate was removed from the combined organics by vacuum filtration, the precipitate was washed thoroughly with EtOAc (4 × 30 mL), and the filtrate was concentrated *in vacuo*. The resultant residue was purified by flash chromatography (SiO_2, petrol/EtOAc, 10:1) to give (±)-5-methyl-2-(prop-1-en-2-yl)hex-5-en-1-ol (±)-**29** (1.89 g, 92%) as a clear oil. Partial data for (±)-**29**: R_f 0.30 (petrol/EtOAc, 4:1); IR (neat) 3347, 3074, 2934, 1647, 1447, 1374, 1042, 885 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.96 (s, 1H), 4.84 (s, 1H), 4.71 (s, 1H), 4.67 (s, 1H), 3.60−3.41 (m, 2H), 2.33−2.23 (m, 1H), 2.03−1.91 (m, 2H), 1.72 (s, 3H), 1.69 (s, 3H), 1.54−1.42 (m, 2H), 1.39 (t, *J* = 5.6, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 145.6, 144.8, 114.1, 110.0, 64.0, 49.5, 35.3, 27.2, 22.5, 18.7; HRMS-ESI (*m/z*) calculated for $C_{10}H_{19}O$ $[M + H]^+$ 155.1430, found 155.1429.

(±)-3-(Iodomethyl)-2,6-dimethylhepta-1,6-diene ((±)-30). To a solution of PPh_3 (5.70 g, 21.8 mmol) and imidazole (1.48 g, 21.8 mmol) in CH_2Cl_2 (100 mL) at 0 °C was added I_2 (5.52 g, 21.8 mmol) portion wise and stirred for 15 min. (±)-**29** (3.05 g, 19.8 mmol) in CH_2Cl_2 (20 mL) was added dropwise, then the reaction mixture was warmed to rt and stirred for 2.5 h. The reaction was quenched by with $Na_2S_2O_3$ solution (11 g in 60 mL of H_2O) and stirred for 10 min, then the product was extracted with CH_2Cl_2 (3 × 50 mL), and the combined organics were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The resultant residue was purified by flash chromatography (SiO_2, neat petrol) to give (±)-3-(iodomethyl)-2,6-dimethylhepta-1,6-diene (±)-**30** (3.71 g, 71%) as a pale orange oil. Data for (±)-**30**: R_f 0.85 (petrol/EtOAc, 4:1); IR (neat) 3074, 2935, 1647, 1445, 1374, 1183, 888 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.92 (s, 1H), 4.78 (s, 1H), 4.72 (s, 1H), 4.68 (s, 1H), 3.21 (ddd, *J* = 17.6, 9.8, 7.2 Hz, 2H), 2.32 (m, 1H), 2.02−1.91 (m, 2H), 1.72 (s, 3H), 1.74−1.68 (m, 1H), 1.66 (s, 3H), 1.55−1.48 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 145.1, 144.9, 113.6, 110.2, 48.9, 35.4, 30.8, 22.4, 18.4, 11.4.

(±)-2-Benzoyl-3,5-dihydroxy-6-(5-methyl-2-(prop-1-en-2-yl)hex-4-en-1-yl)-4,6-bis(3-methylbut-2-en-1-yl)cyclohexa-2,4-dienone ((±)-31). NaH (566 mg, 23.6 mmol) was added portionwise to a solution of **17** (1.24 g, 3.38 mmol) in DMF (30 mL) at rt and stirred for 10 min. Iodide (±)-**30** (5.63 g, 21.3 mmol) was added dropwise, and the reaction mixture was stirred for 30 min before being quenched with satd NH_4Cl (30 mL). The product was extracted with EtOAc (4 × 50 mL), and the combined organics were washed with brine (5 × 100 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The resultant residue was purified by flash chromatography (SiO_2, petrol/EtOAc, 15:1 → 5:1) to give (±)-2-benzoyl-3,5-dihydroxy-6-(5-methyl-2-(prop-1-en-2-yl)hex-4-en-1-yl)-4,6-bis(3-methylbut-2-en-1-yl)cyclohexa-2,4-dienone (±)-**31** (554 mg, 33%) as a viscous yellow oil. Partial data for (±)-**31**: R_f 0.20 (petrol/EtOAc, 4:1); IR(neat) 3408, 2967, 2929, 1662, 1560, 1447, 1376, 909, 888, 731, 696 cm^{-1} NMR spectra showed a complex mixture of tautomers and diastereoisomers; HRMS-ESI (*m/z*) calculated for $C_{33}H_{43}O_4$ $[M + H]^+$ 503.3156, found 503.3156.

(±)-Doitunggarcinone A (2) and (±)-5-*epi*-Doitunggarcinone A (32). To a solution of $Mn(OAc)_3(H_2O)_2$ (591 mg, 2.20 mmol) and $Cu(OAc)_2(H_2O)$ (210 mg, 1.10 mmol) in degassed AcOH (10 mL) was added dropwise a solution of (±)-**31** (554 mg, 1.10 mmol) in degassed AcOH (7 mL) at rt. The reaction mixture was stirred for 3 h and quenched with H_2O (15 mL), and the product was extracted with EtOAc (4 × 50 mL). The combined organics were washed with H_2O (50 mL), satd $NaHCO_3$ (2 × 100 mL), and brine (100 mL), then dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The resultant residue was purified by flash chromatography (SiO_2, petrol/EtOAc, 20:1) to give (±)-doitunggarcinone A (±)-**2** (71 mg, 13%) as an off-white powder. Data for (±)-**2**: R_f 0.53 (petrol/EtOAc, 4:1); mp 221.8−226.4 °C; IR (neat) 3495, 2935, 1736, 1707, 1668, 1450, 1313, 1300, 1255, 1109, 885, 767 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.69 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.54 (td, *J* = 7.6, 1.4 Hz, 1H), 7.36 (td, *J* = 7.6, 0.8 Hz, 1H), 7.35 (d, *J* = 7.6 Hz, 1H), 5.04 (t, *J* = 7.2 Hz, 1H), 4.70 (s, 1H), 4.67 (s, 1H), 2.87 (s, 1H), 2.67 (dd, *J* = 9.9, 7.8 Hz, 1H), 2.27 (d, *J* = 7.1 Hz, 2H), 2.21 (dd, *J* = 13.4, 11.5 Hz, 1H), 2.08 (dd, *J* = 13.4, 11.5 Hz, 1H), 2.09−2.01 (m, 2H), 1.86−1.77 (m, 2H), 1.77 (d, *J* = 14.0 Hz, 1H), 1.75−1.68 (m, 1H), 1.71 (s, 3H), 1.66 (d, *J* = 14.0 Hz, 1H), 1.65 (s, 3H), 1.61−1.55 (m, 1H), 1.57 (s, 3H), 1.49 (m, 1H), 1.44 (s, 3H), 1.36 (s, 3H), 1.09 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 213.2, 203.2, 200.2, 150.1, 145.6, 136.4, 134.4, 133.7, 127.0, 126.4, 123.5, 118.8, 110.1, 91.8, 70.2, 69.2, 63.2, 56.8, 56.4, 47.5, 41.6, 37.2, 36.5, 32.8, 32.6, 29.7, 29.0, 26.2, 25.9, 25.1, 22.5, 18.4, 17.9; HRMS-ESI (*m/z*) calculated for $C_{33}H_{41}O_4$ $[M + H]^+$ 501.2999, found 501.3001. Further elution gave (±)-5-*epi*-doitunggarcinone A (±)-**32** (69 mg, 12%) as an off-white powder. Data for (±)-**32**: R_f 0.50 (petrol/EtOAc, 4:1); mp 210.0−214.0 °C; IR (neat) 3480, 2924, 1734, 1704, 1669, 1452, 1314, 1103, 898, 763 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.70 (dd, *J* = 7.6, 1.3 Hz, 1H), 7.54 (td, *J* = 7.6, 1.4 Hz, 1H), 7.37 (dt, *J* = 7.5, 1.8 Hz, 1H), 7.35 (d, *J* = 7.8 Hz, 1H), 5.08 (t, *J* = 7.3 Hz, 1H), 4.71 (s, 1H), 4.65 (s, 1H), 2.82 (s, 1H), 2.62 (dd, *J* = 9.9, 7.7 Hz, 1H), 2.45 (tt, *J* = 11.8, 3.5 Hz, 1H), 2.28 (d, *J* = 8.0 Hz, 2H), 2.22 (dd, *J* = 11.3, 10.0 Hz, 1H), 2.16 (dd, *J* = 12.3, 10.7 Hz, 1H), 2.07 (dd, *J* = 11.4, 7.7 Hz, 2H), 2.01 (d, *J* = 14.4 Hz, 1H), 1.95−1.89 (m, 1H), 1.69 (s, 3H), 1.65 (s, 3H), 1.58 (s, 3H), 1.45 (s, 3H), 1.44 (d, J = 14.4 Hz, 1H), 1.45−1.33 (m, 2H), 1.36 (s, 3H), 1.10 (s, 3H) 1.08−1.02 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 213.4, 203.2, 200.2, 150.2, 145.2, 136.4, 134.6, 133.7, 127.0, 126.4, 123.5, 118.9, 110.2. 91.7, 71.1, 69.0, 62.9, 56.2, 51.7, 42.5, 37.2, 36.8, 35.1, 31.3, 29.8, 29.7, 29.5, 26.2, 25.8, 24.8, 22.6, 22.4, 17.9; HRMS-ESI (*m/z*) calculated for $C_{33}H_{41}O_4$ $[M + H]^+$ 501.2999, found 501.3001.

Phenyl(2,4,6-trihydroxy-3,5-diisopentylphenyl)methanone (33). To a solution of **17** (1.20 g, 3.27 mmol) in EtOH (40 mL) was added Pd/C (50 mg) at rt. The flask was evacuated three times and placed under an atmosphere of H_2. The reaction mixture was stirred at rt for 2 h. The mixture was filtered through a pad of Celite extracting with EtOAc, and the filtrate was concentrated *in vacuo*. The residue was purified by flash chromatography on SiO_2 (petrol/EtOAc, 6:1 as elutant) to give phenyl(2,4,6-trihydroxy-3,5-diisopentylphenyl)-methanone **33** (950 mg, 79%) as a yellow crystalline solid. Data for **33**: R_f 0.49 (petrol/EtOAc, 4:1); IR (neat) 3505, 2949, 1621, 1561, 1314, 1191, 1092, 926, 698 cm^{-1}; mp 82−83 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.80 (s, 1H), 7.64 (d, *J* = 7.1 Hz, 2H), 7.59 (t, *J* = 7.4 Hz, 1H), 7.53 (t, *J* = 7.6 Hz, 2H), 5.40 (s, 1H), 2.54 (dt, *J* = 14.7, 6.0 Hz, 4H), 1.65−1.55 (m, 2H), 1.40−1.34 (m, 4H), 0.95 (s, 3H), 0.94 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 197.6, 159.6, 157.4, 139.9, 132.3, 129.4, 127.8, 107.8, 104.4, 38.1, 28.2, 22.5, 20.7; HRMS-ESI (*m/z*) calculated for $C_{23}H_{31}O_4$ $[M + H]^+$ 371.2217, found 371.2221.

2-Benzoyl-3,5-dihydroxy-4,6-diisopentyl-6-(3-methylbut-3-en-1-yl)cyclohexa-2,4-dienone (34). To a solution of **33** (409 mg, 1.10 mmol) in anhydrous DMF (10 mL) was added NaH (80 mg, 3.3 mmol) at rt. The mixture was stirred at rt for 5 min before 4-iodo-2-methyl-1-butene **12** (0.26 mL, 2.20 mmol) was then added at rt. The reaction mixture was stirred at rt for 1 h. The mixture was quenched with 1 M HCl solution (10 mL) and extracted with EtOAc (3 × 15 mL). The combined organics were washed sequentially with H_2O (2 × 30 mL) and brine (30 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by flash chromatography on SiO_2 (petrol/EtOAc, 8:1) to give 2-benzoyl-3,5-dihydroxy-4,6-diisopentyl-6-(3-methylbut-3-en-1-yl)cyclohexa-2,4-dienone **34** (177 mg, 37%) as an off white solid. Data for **34**: R_f 0.28 (petrol/EtOAc, 4:1); mp 116−119 °C; IR (neat) 3187, 2956, 1646, 1447, 1207, 1171, 692 cm^{-1}; NMR spectra showed a complex mixture of tautomers; HRMS-ESI (m/z) calculated for $C_{28}H_{39}O_4$ $[M + H]^+$ 439.2843, found 439.2847.

ASSOCIATED CONTENT

Supporting Information

^{1}H and ^{13}C NMR spectra for compounds **1**, **2**, **10**, **11**, **13**, **16**−**19**, **21**−**25**, and **27**−**34** and chiral HPLC traces for (+)-**1**, (−)-**1**, and (±)-**1**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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